

**Food and Drug Administration**  
**FY 2013 Congressional Budget Request**  
Table of Contents

	<b><u>Page</u></b>
<b><u>Significant Items:</u></b>	
Item 1 – Spending Plans	<b>573</b>
Item 2 – Food Safety Research	<b>573</b>
Item 3 – Trade Facilitation & Interagency Cooperation	<b>574</b>
Item 4 – Independent Post-Market Surveillance	<b>574</b>
Item 5 – Pediatric Devices	<b>574</b>
Item 6 – Influenza Vaccines	<b>574</b>
Item 7 – Pediatric Cancer	<b>575</b>
Item 8 – Sunscreen	<b>576</b>
Item 9 – Gluten-free Rulemaking	<b>577</b>
Item 10 – OTC Cold Medicines for Children	<b>578</b>
Item 11 – Medical Devices Advisory Committee	<b>578</b>
Item 12 – Seafood Advisory	<b>579</b>
Item 13 – Nutrition Labeling	<b>579</b>
Item 14 – FDA Spending	<b>580</b>
Item 15 – FSMA	<b>581</b>
Item 16 – MCM	<b>581</b>
Item 17	<b>581</b>
Item 18 – Adjuvanted Influenza Vaccines	<b>582</b>
Item 19 – Agency Collaboration	<b>583</b>
Item 20 – Antimicrobial Resistance	<b>583</b>
Item 21 – Artificial Pancreas	<b>584</b>
Item 22 – Breast Imaging Quality Standards	<b>585</b>
Item 23 – Budget Justification	<b>585</b>
Item 24 – Dietary Supplements	<b>586</b>
Item 25 – Food Safety Information Sharing	<b>586</b>
Item 26 – Generic Drugs	<b>587</b>
Item 27 – Medical Device Safety	<b>587</b>
Item 28 – GAO Recommendations	<b>588</b>
Item 29 – Nanotechnology	<b>589</b>
Item 30 – Obesity Therapeutics	<b>589</b>
Item 31 – Office of Cosmetics and Colors [OCAC]	<b>590</b>
Item 32 – Packaged Ice	<b>590</b>
Item 33 – Seafood Advisory	<b>591</b>
Item 34 – Seafood Economic Integrity	<b>591</b>
Item 35 – Seafood Safety	<b>591</b>

<b>Item 36 – Trade Facilitation and Interagency Cooperation</b>	<b>592</b>
<b>Item 37 – Administrative Savings</b>	<b>593</b>
<b>Item 38 – Pre-Market Approval Times</b>	<b>593</b>
<b>Item 39 – OTC Cold Medicines for Children</b>	<b>593</b>
<b>Item 40 – Nanotechnology</b>	<b>594</b>
<b>Item 41 – Imported Seafood</b>	<b>594</b>
<b>Item 42 – Approval Process transparency</b>	<b>595</b>
<b>Item 43 – Food Safety</b>	<b>595</b>

**Food and Drug Administration  
House and Senate FY 2013  
Significant Items**

**House Significant Items  
Contained in House Report 112-101  
June 3, 2011**

**Item 1 – Spending Plans** – Within 30 days from the enactment of this Act, the Commissioner shall notify the Committees on Appropriations of both Houses of Congress, on the allocation of the funds provided herein by account, and within each account by program, project and activity. (p.51) (DBEC)

**FDA Action**

On January 5, 2012, FDA provided the 30-day report that the Committee requested.

**Item 2 – Food Safety Research** – The Committee urges FDA to collaborate on its research needs where possible to reduce redundancy regarding food safety research in produce and to find efficiencies where possible when constructing new research facilities. (p.51)

**FDA Action**

FDA has developed three, cascading strategic plans to organize and coordinate food safety research: the FDA-wide Advancing Regulatory Science (ARS) Strategic Plan, released August 2011, the Foods Program draft Food and Veterinary Medicine (FVM) Strategic Plan, released for public comment in September 2011, and the Strategic Plan for CFSAN Science and Research (CSR), released November 2010. For example, the CSR plan directly supports the achievement of ARS plan Goal 6, “Implement a New Prevention-Focused Food Safety System to Protect Public Health,” and FVM Strategic Plan Program Goal 3, “Strengthen scientific leadership, capacity, and partnership to support public health and animal health decision making.”

FDA uses its strategic plans to target and coordinate regulatory science resources for food safety across the Agency on mission-driven priority areas, such as produce safety. The CSR plan identifies seven areas of high priority research needed to support the proposed produce safety rule. CFSAN uses the plan as a basis for prioritizing and coordinating research projects among its research and program offices, as well as with CVM and ORA. All projects are assigned leads and evaluated against specific timelines under the auspices of the CFSAN Senior Science Advisor and the Office of Foods.

Produce safety research is also conducted by extramural research partners, such as the Western Center for Food Safety (WCFS), which was established in 2008 by an FDA cooperative agreement with the Western Institute for Food Safety and Security (WIFSS) of the University of California, Davis. By engaging external Centers of Excellence on high-priority research projects, such as produce safety, FDA is able to achieve significant efficiencies in conducting research by reducing redundancy and the cost of research facilities.

**Item 3 – Trade Facilitation & Interagency Cooperation** –The current fiscal environment requires that efforts to enhance safety must be directed towards the most serious compliance infractions. The Committee strongly encourages FDA to establish a pilot project to expedite imports for highly compliant importers. Such project could be modeled on the Customs and Border Protection (CBP) Customs- Trade Partnership Against Terrorism and Importer Self-Assessment programs. The goal would be new trade facilitation methods for low-risk, shippers and cargo that could be incorporated into the import inspection process, thereby enabling FDA to better target Federal resources. FDA is strongly encouraged to provide clear guidelines for those shippers who are low-risk and to collaborate with CBP and other relevant agencies on this work. FDA is directed to provide a report to the Committee on its efforts in this regard by December 1, 2011. (p.52) (ORA)

**FDA Action**

FDA will provide the report that the Committee requested.

**Item 4 – Independent Post-Market Surveillance** – Concerns have been raised that those at FDA who approve drugs also have a large role in determining how they are regulated for safety in post-marketing surveillance. The Committee directs FDA to issue a report by March 31, 2012, that would outline the process necessary to create an independent office within the agency that is focused on postmarket evaluation with the controls and separation of duties necessary to make unbiased decisions on safety and advocacy. This process should also ensure that the post-market surveillance and pre-market functions can work collaboratively so that science-based, post-market assessments can formally feed back to officials involved with making pre-market drug approvals. (p.52)

**FDA Action**

FDA will provide the report that the Committee requested.

**Item 5 – Pediatric Devices** – The Committee supports FDA's efforts in addressing the need for improved pediatric medical devices. Since the inception of Demonstration Grants for Improving Pediatric Device Availability, four

consortia funded by the Office of Orphan Products Development have assisted in the development of more than 80 potential pediatric devices. While the Committee does not have additional resources to provide an increase, the Committee directs that FDA maintain level funding for this program. (p.52)

#### **FDA Action**

Subject to any changes to the FDA appropriation after the enactment of P.L. 112-55, FDA will maintain level funding for this program as requested by the committee.

**Item 6 – Influenza Vaccines** – The Committee is aware FDA has not yet exercised its authority under the Accelerated Approval of Biological Products regulation to approve licenses for adjuvanted seasonal influenza vaccines that have a proven safety record. While discussions about licensing such a vaccine have been ongoing at FDA, no pathway for approval has been established. The Committee believes FDA has the authority to approve these vaccines and encourages FDA to exercise that authority. The Committee is also aware that clinical studies are needed to further the development of new treatments for emerging public health requirements and for pandemic preparedness. The Committee urges FDA to work with interagency partners to ensure funding is available to conduct these needed clinical studies. (p.52)

#### **FDA Action**

The approval pathways for adjuvanted seasonal vaccines do not differ from those for unadjuvanted seasonal influenza vaccines.

Under the traditional approval pathway, an adjuvanted seasonal influenza vaccine can be licensed provided that the applicant has demonstrated safety and effectiveness through adequate and well controlled clinical trials in the proposed target population and has submitted a biologics license application. Under the accelerated approval process, licensure is based on a demonstration of an immune response, which is a surrogate endpoint reasonably likely to predict clinical benefit. This approval is contingent upon the applicant studying the vaccine further to verify and describe its actual clinical benefit. The accelerated approval process is available for adjuvanted influenza vaccines.

In 2007, FDA issued guidance documents on seasonal and pandemic influenza vaccines that also address adjuvants. Copies of these guidance documents can be found on FDA's website at:

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm074794.htm> and

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm074786.htm>

For the 2009 H1N1 pandemic vaccine, clinical data from studies supported by the Department of Health and Human Services (DHHS) and manufacturers showed that currently approved standard doses of non-adjuvanted licensed vaccines induced an excellent immune response against the 2009 H1N1 virus and an adjuvanted influenza vaccine was not necessary. In the United States the ability to use licensed influenza vaccines, which have an extensive record of safe and effective use, contributed to public confidence in and use of the 2009 H1N1 vaccines. However, to prepare for a greater public health emergency in response to the H1N1 pandemic, the DHHS stockpiled adjuvant and the DHHS and FDA were prepared to allow the use of unlicensed adjuvanted vaccines under emergency-use authorization. The scientific leadership of HHS agencies met periodically to consider this and repeatedly determined that the use of non-adjuvanted licensed vaccines was appropriate for the public health response to the H1N1 pandemic.

Studies are currently underway to determine whether the addition of adjuvants to trivalent inactivated seasonal influenza vaccines enhances their effectiveness. Some of these studies have received support from DHHS. Because seasonal vaccines are administered to over 100 million people every year, including young children and pregnant women, it is important to ensure that adjuvanted seasonal influenza vaccines will have an excellent safety profile, similar to currently licensed seasonal influenza vaccines.

The FDA has met with and provided advice and guidance to manufacturers that have submitted investigational new drug applications for adjuvanted seasonal influenza vaccines to ensure the availability of the needed safety and efficacy data.

**Item 7 – Pediatric Cancer** – The Committee notes cancer remains the leading cause of disease-related death in children. The incidence of childhood cancer is increasing and more effective and less toxic treatments are needed. The Committee recognizes that only one drug has been approved for pediatric cancer in the last twenty years. The Committee encourages FDA to collaborate with industry and the pediatric cancer community to promote the development of new therapies. (p.52)

#### **FDA Action**

FDA continues to prioritize interactions with sponsors (pharmaceutical companies), the National Institutes of Health, the European Medicines Agency and other academic partners on new treatment options for pediatric cancer patients.

FDA issued a specific guidance for sponsors on how to participate in the Best Pharmaceuticals for Children Act (BPCA) incentive program for the development of products directed to treat pediatric cancers.

BPCA encourages development of products for treating pediatric cancer patients through granting product exclusivity based on limited clinical development.

To date, FDA has granted exclusivity and expanded labeling under BPCA for the following drugs used for treatment of pediatric patients with cancer: Afinitor (10/2010), Gleevec (9/2006), Arranon (10/2005), Zofran (3/2005), Busulfex (1/2003), Clolar (12/2004) and Elitek (7/2002). Additionally, outside of BPCA the following drugs have FDA approval for use in pediatric cancer treatment: Elspar (3/2007), Oncaspar (7/2006) and Erwinaze (11/2011).

Informative labeling changes to assure safe and effective use of the following nine drugs for pediatric cancer have been made since 2000: Vinorelbine, Temozolomide, Topotecan, Fludarabine, Irinotecan, Gemcitabine, Oxaliplatin, Docetaxel, and Fludarabine.

Also, FDA's Center for Drug Evaluation and Research's Office of Hematology and Oncology Products initiated biennial meetings of the FDA's pediatric subcommittee of the Oncologic Drugs Advisory Committee to facilitate review and discussion of potential development plans for select new drugs in the pediatric population.

**Item 8 – Sunscreen** – In August 2007, FDA published a proposed rule for over-the-counter sunscreens that would require UVB and UVA testing and labeling. Given the importance of this rule to protecting Americans against skin cancer, the Committee is concerned that FDA has not issued a final rule. The Committee instructs FDA to issue a final rule before December 31, 2011. (p.53)

#### **FDA Action**

On June 17, 2011, FDA published the new sunscreen Final Rule to address UVB and UVA efficacy testing and labeling for sunscreen products as well as skin cancer labeling statements that are dependent on the degree of sun protection provided by the product.

**Item 9 – Gluten-free Rulemaking** – Public Law 108–282 required a final rule to define and permit the use of the term “gluten-free” on food labels not later than August 2008. Given the importance of this rule to protecting consumers, the Committee is concerned that FDA has not issued a final rule. The Committee instructs FDA to issue a final rule before December 31, 2011. (p.53)

#### **FDA Action**

FDA recognizes the importance of issuing a final rule on gluten-free food labeling as quickly as possible, and fully intends to achieve this goal. To develop an effective, science-based standard, FDA recently reopened the comment period

on the proposed rule to release the Agency's safety assessment on gluten exposure in persons with celiac disease and solicit comments on it. The comment period closed on October 3, 2011 and FDA received more than 1,300 comments. It was not possible for FDA to review all of these comments, complete the rulemaking process, and publish a final rule by December 31, 2011. However, FDA intends to publish by the end of FY 2012 a final rule that will establish a regulatory definition of the food labeling term "gluten-free."

**Item 10 – OTC Cold Medicines for Children** –The Committee is concerned that FDA has not issued a proposed rule revising the monograph regulating the labeling of over-the-counter cough and cold products for children. The Committee directs the agency to publish a proposed rule by December 31, 2011, based on scientific evidence for safety and efficacy in pediatric populations and consistent with the October 19, 2007, joint recommendations of its Pediatric Advisory Committee and Nonprescription Drugs Advisory Committee. (p.53)

#### **FDA Action**

FDA acknowledges the importance of issuing a proposed rule addressing potential changes to the labeling of over-the-counter cold and cough products for use in children. Although the changes being considered are very complex and require appropriate justifications, the FDA is working expeditiously to issue this proposed rule.

**Item 11 – Medical Devices Advisory Committee** –The Committee commends FDA for convening the General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee in March 2010 to review the medical device classification of tanning beds. The Committee encourages the agency to act in a timely fashion to finalize its review and make formal recommendations regarding this classification. (p.53)

#### **FDA Action**

The General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee convened in March, 2011 to receive testimony from more than 50 professional societies, industry representatives, melanoma survivors or family members of melanoma victims, and other interested parties on the public health issues surrounding tanning lamps. The expert panel reached a consensus that tanning beds/lamps should be up-classified from their current Class I medical device status to provide greater scrutiny of the safety and effectiveness of these devices. A majority of the panel also favored restricting tanning lamps to adult use and disclosing more information on the risks of tanning to consumers.

FDA is reviewing the Advisory Committee's recommendations to reclassify tanning lamps and determine who should and should not use the devices. The

Agency is also evaluating additional controls based on the Advisory Committee's recommendations.

FDA is developing a regulation to amend current performance standards for tanning lamps to assure their safety and safe use.

**Item 12 – Seafood Advisory** –The Committee is concerned about differing messages from Federal agencies to pregnant women regarding the nutritional value of seafood consumption during pregnancy. The Committee directs FDA to initiate formal reconsideration of the 2004 advisory in consideration of the 2010 Dietary Guidelines. FDA shall report to the Committee within 90 days of enactment of this Act on progress made and a timeline for final action on a new FDA advisory. (p.53)

#### **FDA Action**

FDA is discussing with the Environmental Protection Agency (EPA) an update of the 2004 advisory regarding the nutritional value of seafood consumption during pregnancy, in light of, among other things, a net benefits assessment conducted by FDA and the 2010 Dietary Guidelines. The agencies intend to issue a draft of an updated advisory early this year and then engage the public on this topic through public meetings and comments this year. This may include a consultation with the FDA Advisory Committee on Risk Communication.

**Item 13 – Nutrition Labeling** –The Committee is concerned with the proposed rule that FDA issued on April 6, 2011, on nutrition labeling of standard menu items in restaurants and similar retail food establishments. The proposed rule would include establishments that are not primarily in the business of selling food for immediate consumption or selling food that is prepared or processed on the premises. These establishments are not similar to restaurants and the Committee believes that FDA should define the term “restaurant” to mean only restaurants doing business marketed under the same name or retail establishments where the primary business is the selling of food for immediate consumption. The Committee urges FDA to use the proposed alternative definition in the rule that would encompass only establishments where the primary business is the selling of food for immediate consumption or selling food that is prepared and processed on the premises. (p.53)

#### **FDA Action**

FDA is aware of the Committee's concerns about FDA's definition of “restaurant and similar retail food establishment” and the Committee's support for FDA's alternate definition in the proposed rule that would encompass only establishments where the primary business is the selling of food for immediate consumption or selling food that is prepared and processed on the premises. FDA received many comments on the proposed definition of “restaurant and

similar retail food establishment,” ranging from comments similar to the Committee’s, comments supporting FDA’s proposed definition, and comments supporting a definition to include all facilities that serve restaurant and restaurant-type foods. FDA is proceeding in a deliberative manner to ensure that all comments are fully evaluated and their views considered before a final regulation is issued.

**Item 14 – FDA Spending** – The Committee is deeply troubled about the expenditure of scarce appropriated funds investigating alleged use of performance enhancing drugs. The Committee can discern no prudent interest for the FDA to investigate allegations that unapproved drugs may have been used outside the United States, where there is no allegation that they were sought to be imported into the U.S. and no risks to public health in the U.S. It exemplifies the problems identified by the GAO in 2010, which found that the FDA has failed to exercise appropriate oversight of the Office of Criminal Investigation or to ensure that its activities are consistent with the FDA’s mission and priorities. The Committee takes no position on the merits of any pending allegations, but holds concerns about the use of taxpayer funds for investigations falling outside the agency’s core missions. (p.53)

#### **FDA Action**

The illegal distribution of misbranded and unapproved drugs, which are often foreign sourced, diverted, and/or counterfeit, are prohibited criminal violations under the Food, Drug and Cosmetic Act. These violations are serious crimes with dangerous public health consequences. Performance enhancing drugs, which are typically foreign sourced, remain a concern at FDA as they are a distinct public health issue, particularly to a very vulnerable element of our society, our nation’s youth. FDA does not investigate allegations involving unapproved drugs used outside the United States, where there is no allegation of an attempt to introduce the drugs into U.S. commerce.

FDA Commissioner Hamburg addressed the concerns raised by the 2010 GAO report in her March 11, 2011 appearance before Congressman Jack Kingston, Chairman Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and related agencies. FDA has a series of procedures, adopted in 2010, to ensure that the priorities of OCI and the rest of FDA are aligned. These procedures, which are set forth in FDA Staff Manual Guides and its Regulatory Procedures Manual, provide for regular coordination of Agency priorities between OCI and each of the Agency’s Centers.

**Senate Significant Items  
Contained in Senate Report  
Number 112-73  
Date September 7, 2011**

**Item 15 – FSMA** –The Committee recommendation includes an increase of \$40,000,000 for FDA to begin implementation of the Food Safety Modernization Act [FSMA]. This legislation will establish a prevention- focused food safety system and leverage the work of FDA’s State and local food safety partners. Due to budgetary constraints, the Committee was unable to provide the full funding request for implementation of FSMA, and directs FDA to apply these increased funds to the highest priority food safety activities. These activities could include publication of new preventative controls for food processing facilities, additional import oversight and inspections of both foreign and domestic facilities, and improved scientific capabilities. The Committee directs FDA to provide a report within 30 days of enactment of this act on how it intends to allocate these funds.

**FDA Action**

On January 5, 2012, FDA provided the 30-day report that the Committee requested.

**Item 16 – MCM** – The Committee also provides an increase of \$19,038,000 for activities relating to advancing medical countermeasures. This initiative was begun in August 2010 in order to increase the U.S. readiness against public health threats, and will allow FDA to work with other Government agencies to facilitate the development of safe and effective medical countermeasures to protect the Nation from chemical, biological, radiological, nuclear, and emerging infectious disease threats. Again, due to budgetary constraints, the Committee was unable to provide the full funding request for these activities, and directs FDA to provide funding to the highest priority activities relating to these initiatives. The Committee directs FDA to provide a report within 30 days of enactment of this act on how it intends to allocate these funds.

**FDA Action**

On **January 3, 2012**, FDA provided the 30-day report that the Committee requested.

**Item 17** – The Committee expects FDA to continue all projects, activities, laboratories, and programs as included in the fiscal year 2012 budget request, unless otherwise specified.

### **FDA Action**

Subject to any changes to the FDA appropriation after the enactment of P.L. 112-55, FDA will continue all projects, activities, laboratories, and programs as included in the fiscal year 2012 budget request at the funding level recommended by the Committee.

**Item 18 – Adjuvanted Influenza Vaccines** – The Committee recognizes the importance of FDA exercising its authority under the Accelerated Approval of Biological Products regulation to approve licenses for adjuvanted seasonal influenza vaccines, which are currently being used in seasonal influenza campaigns in Europe. The Committee believes that FDA has sufficient authority under existing regulations to approve adjuvanted vaccines. The Committee is also aware that adjuvanted seasonal influenza clinical studies are needed to further encourage the development of new treatments for emerging public health requirements and for pandemic preparedness. The Committee urges the FDA to work collaboratively with industry and other Federal agencies to facilitate the design and conduct the necessary studies. (p.80)

### **FDA Action**

The approval pathways for adjuvanted seasonal vaccines do not differ from those for unadjuvanted seasonal influenza vaccines.

Under the traditional approval pathway, an adjuvanted seasonal influenza vaccine can be licensed provided that the applicant has demonstrated safety and effectiveness through adequate and well controlled clinical trials in the proposed target population and has submitted a biologics license application. Under the accelerated approval process, licensure is based on a demonstration of an immune response, which is a surrogate endpoint reasonably likely to predict clinical benefit. This approval is contingent upon the applicant studying the vaccine further to verify and describe its actual clinical benefit. The accelerated approval process is available for adjuvanted influenza vaccines.

In 2007, FDA issued guidance documents on seasonal and pandemic influenza vaccines that also address adjuvants. Copies of these guidance documents can be found on FDA's website at:

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm074794.htm> and

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm074786.htm>

For the 2009 H1N1 pandemic vaccine, clinical data from studies supported by the Department of Health and Human Services (DHHS) and manufacturers showed that currently approved standard doses of non-adjuvanted licensed vaccines induced an excellent immune response against the 2009 H1N1 virus and an adjuvanted influenza vaccine was not necessary. In the United States

the ability to use licensed influenza vaccines, which have an extensive record of safe and effective use, contributed to public confidence in and use of the 2009 H1N1 vaccines. However, to prepare for a greater public health emergency in response to the H1N1 pandemic, the DHHS stockpiled adjuvant and the DHHS and FDA were prepared to allow the use of unlicensed adjuvanted vaccines under emergency-use authorization. The scientific leadership of HHS agencies met periodically to consider this and repeatedly determined that the use of non-adjuvanted licensed vaccines was appropriate for the public health response to the H1N1 pandemic.

Studies are currently underway to determine whether the addition of adjuvants to trivalent inactivated seasonal influenza vaccines enhances their effectiveness. Some of these studies have received support from DHHS. Because seasonal vaccines are administered to over 100 million people every year, including young children and pregnant women, it is important to ensure that adjuvanted seasonal influenza vaccines will have an excellent safety profile, similar to currently licensed seasonal influenza vaccines.

The FDA has met with and provided advice and guidance to manufacturers that have submitted investigational new drug applications for adjuvanted seasonal influenza vaccines to ensure the availability of the needed safety and efficacy data.

**Item 19 – Agency Collaboration** – The Committee is aware of the MOU between FDA and the Centers for Medicare and Medicaid Services [CMS] to promote collaboration, and strongly supports this effort. The Committee encourages FDA to share information with CMS describing the clinical trials used to support a new drug indication, and to specifically note whether the new drug was compared to a placebo or to an active control. The Committee recommends that FDA make CMS aware of whether a newly approved drug was approved based on an application supported by clinical trials using a non-inferiority or a superiority design. (p.80)

#### **FDA Action**

FDA and CMS are currently sharing information under this MOU. FDA will take these recommendations into consideration as we continue to collaborate with CMS.

**Item 20 – Antimicrobial Resistance** – The Committee commends the FDA for publishing Draft Guidance for Industry No. 209 and for conducting a comprehensive review of the scientific evidence related to antimicrobial use in food animal production and antibiotic-resistant infections in humans. However, over a year has passed since this draft guidance was released and the FDA has not yet identified a timeframe for finalizing and implementing this guidance or for taking other proposed steps to address antimicrobial resistance. Therefore,

the Committee directs the FDA to set a timeline for when Guidance No. 209 and any implementing guidance will be finalized, when the FDA intends to release any changes to the Veterinary Feed Directive, and when it plans to issue an order regarding extra label uses of Cephalosporin drugs in food-producing animals. The Committee also recommends that FDA examine medically important antimicrobial drugs currently approved for use in food-producing animals and take steps to assure that such products are aligned with current safety standards. (p.80)

### **FDA Action**

FDA recognizes the important public health implications of this issue and has been actively taking steps to address this safety concern.

FDA has completed a review of the public comments received on draft Guidance for Industry #209 and is developing a strategy for implementing the recommendations outlined in the draft guidance. This includes seeking input from its stakeholders, including the animal pharmaceutical industry, on approaches for voluntarily modifying medically important antimicrobial drugs currently approved for use in food-producing animals to limit their use to therapeutic purposes under veterinary oversight.

Furthermore, as comments on the guidance are being reviewed, FDA is working with a number of individual pharmaceutical companies that have approached the agency on a case-by-case basis to examine their particular products and discuss possible changes to their products to address antimicrobial resistance concerns. FDA is encouraged by the engagement of the animal pharmaceutical industry and their commitment to work cooperatively with the agency to address this issue.

Finalizing the various elements of FDA's strategy for addressing antimicrobial resistance continues to be a high priority for the Agency. FDA expects to move forward with elements of the plan in early 2012.

**Item 21 – Artificial Pancreas** –To foster the development of artificial pancreas technology, the Committee expects FDA to provide researchers and industry stakeholders with clear, prompt, and reasonable guidance for approval of safe and effective artificial pancreas systems for patients with type I diabetes. The FDA has taken an important first step with the issuance of guidance for an early version of an artificial pancreas system, known as a Low Glucose Suspend system. The Committee strongly encourages FDA to continue to make the advancement of more autonomous artificial pancreas technologies a priority by collaboration with stakeholders and investment of time and resources. Artificial pancreas technologies could be an important tool for patients with type 1 diabetes to achieve better glycemic control, increasing their quality of life and overall health. (p.80)

### **FDA Action**

On December 1, FDA issued draft guidance designed to help investigators and manufacturers develop and seek approval for artificial pancreas device systems to treat type 1 diabetes. The draft guidance provides flexible recommendations for design and testing that meet statutory requirements for safety and effectiveness.

An artificial pancreas could reduce dangerous high and low blood sugars, providing a better quality of life for millions of Americans with diabetes and lower the risk for future diabetes-related complications.

The guidance recommends a three-phase clinical study progression so that studies may move to an outpatient setting as quickly as possible. To further streamline clinical studies, the guidance suggests ways sponsors may leverage existing safety and effectiveness data for components that may make up an artificial pancreas system, as well as data gathered from clinical studies conducted outside of the U.S.

FDA looks forward to reviewing comments from industry and other interested parties on the draft guidance to facilitate evaluation and review of the safety and effectiveness of this promising technology. The agency is committed to ensuring that the devices that become available that utilize this technology provide a favorable benefit to risk profile for the patients that use them.

**Item 22 – Breast Imaging Quality Standards** – The Committee is aware that FDA is currently considering the implementation of several recommendations included in the Institute of Medicine Report entitled “Breast Imaging Quality Standards”, which was released on May 23, 2005. The Committee directs FDA to provide a report to the House and Senate Committees on Appropriations within 120 days of enactment of this act specifying which specific recommendations will be implemented, the timeline for doing so, and specific details on how the recommendations will be implemented. (p.81)

### **FDA Action**

FDA will provide the report that the Committee requested.

**Item 23 – Budget Justification** – The Committee directs FDA to submit the fiscal year 2013 budget request in a format that follows the same account structure as the fiscal year 2012 budget request unless otherwise approved by the Committee. (p.81)

**FDA Action**

FDA will submit the fiscal year 2013 budget request in a format that follows the same account structure as the fiscal year 2012 budget request unless otherwise approved by the Committee

**Item 24 – Dietary Supplements** – The Committee is aware that U.S. consumers widely use plant-derived dietary supplements, and that FDA inspects manufacturers and distributors that are responsible for ensuring that such products are not adulterated or contaminated, and do not cause harm to the consumer. The Committee believes that methods and standards are needed to verify source plants and ingredients and to detect toxic contaminants. The Committee encourages FDA to develop guidance for industry on such methods and standards, which would enhance FDA's ability to inspect and assess industry practices for manufacturing botanical dietary supplements. (p.81)

**FDA Action**

FDA currently partners with academic and industry stakeholders to support development of methods and standards for manufacturing botanical dietary supplements. These agreements allow FDA to establish broad-based initiatives that enhance FDA's ability to protect overall public health by ensuring that dietary supplements are safe and their labeling is truthful and not misleading.

One example is the FDA agreement with the National Center for Natural Products Research (NCNPR) at the University of Mississippi. This collaboration creates a partnership that allows for more efficient use of botanical dietary supplements research resources in investigating potentially toxic botanical ingredients and constituents. Additionally, publications and meetings with academic and industry partners regarding best practices, including those for analysis of specific components of botanical dietary supplements, effectively provide scientific guidance for FDA and industry alike in setting and assessing industry practices for manufacturing botanical dietary supplements.

**Item 25 – Food Safety Information Sharing** – The Committee urges the Secretary of Agriculture and the Secretary of Health and Human Services to enter into a memorandum of understanding between the relevant agencies within the Department of Health and Human Services, including the Food and Drug Administration and the Centers for Disease Control and Prevention, and the relevant agencies within the Department of Agriculture, including the Food Safety and Inspection Service, the Agricultural Research Service, and the Animal and Plant Health Inspection Service, to ensure the timely and efficient sharing of all information collected by such agencies related to foodborne pathogens, contaminants and illnesses. (p.81)

### **FDA Action**

FDA has entered into a large number of cooperative agreements with several other departments within the Executive Branch, including the Department of Agriculture, the Department of Defense, and the Department of Homeland Security, as well as agencies such as the Environmental Protection Agency (EPA). FDA is ever-vigilant for new means of cooperation between agencies and is diligent about ensuring that agreements are updated as necessary. For example, FDA entered into an MOU (225-72-2009) last year with USDA's Agriculture Marketing Service (AMS), which is designed to ensure maximum coordination and cooperation between AMS and FDA with respect to information-sharing on food safety, including produce and egg safety. Additionally, FDA has entered in an MOU with USDA's Research, Education, and Economics (REE) to establish a cooperative program with the National Institute for Food and Agriculture (NIFA) to provide training as mandated by the Food Safety Modernization Act. FDA is also currently finalizing revisions to an existing MOU between FDA, USDA, and EPA relative to the sharing of information on residues and chemical contaminants in foods. A full listing of such agreements, including additional examples of FDA food safety data-sharing, can be found at: <http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/default.htm>.

**Item 26 – Generic Drugs** – The Committee recommendation includes no less than \$97,218,000 for the generic drugs program at FDA, of which no less than \$52,947,000 is for the Office of Generic Drugs. (p.81)

### **FDA Action**

Subject to any changes to the FDA appropriation after the enactment of P.L. 112-55, during FY 2012, FDA will support this activity at the funding level recommended by the Committee.

**Item 27 – Medical Device Safety** – The Committee strongly encourages the Center for Devices and Radiological Health [CDRH] to complete its implementation of the Safe Medical Devices Act of 1990. The Government Accountability Office [GAO] identified the unfinished implementation of this act as one of the main causes of including CDRH on GAO's "high-risk" list of Government agencies. The Committee directs CDRH to report on its progress of the implementation of the Safe Medical Devices Act within 120 days of the enactment of this act. (p.81)

### **FDA Action**

FDA will provide the report that the Committee requested.

**Item 28 – GAO Recommendations** – The Committee also encourages CDRH to implement the GAO recommendation for CDRH to strengthen its post-market surveillance of medical devices. The Committee supports CDRH's use of Section 522 authority to study high-risk medical devices that were cleared through the 510(k) process, such as metal-on-metal hip implants. The Committee commends CDRH on meeting with medical experts and leaders of medical device registries that currently exist and recommends that CDRH continue to work with stakeholders to develop a more robust post-market surveillance program for medical devices. (p.81)

### **FDA Action**

FDA has stepped up its postmarket device surveillance efforts and engaged with a wide spectrum of stakeholders to identify safety signals as early as possible and take appropriate action. These efforts include combining and leveraging advances in epidemiology, statistics, and biomedical research to assess medical device safety and effectiveness through the Medical Device Epidemiology Network (MDEpiNet). As part of the MDEpiNet Initiative, FDA held a general public meeting and three targeted workshops with diagnostics, orthopedics, and surgical device stakeholders. In addition, a Science/Infrastructure Center and Methodology Center were established at two of our partner academic institutions to facilitate more informed decision-making about medical devices.

Access to already established data sources through device registries is an essential complement to monitor device performance in a timely and cost effective manner. FDA has played an important role in the development of the infrastructure needed for appropriate postmarket surveillance of medical devices through device registries. In 2011, FDA facilitated development of the American College of Cardiology/Society of Thoracic Surgeons (ACC/STS) Transcatheter Valve Therapy Registry and engaged in further infrastructure building for the International Consortium of Orthopedic Registries (ICOR), the ICD and Leads registries (held by ACC/STS), and the Kaiser family of registries. We will continue to engage in collaborations with US and international professional organizations, academia, and the medical device industry to develop better systems for postmarket surveillance. MDEpiNet provides the platform for such collaborations.

Postmarket surveillance under section 522 of the Federal Food, Drug, and Cosmetic Act is an integral component of our postmarket surveillance toolkit. Study plans are submitted by sponsors and must be approved by FDA prior to study initiation. In 2011, FDA issued 149 "522 orders" for three device areas up from 13 orders for two device areas issued in the prior year.

**Item 29 – Nanotechnology** – The Committee recognizes that FDA is developing the facilities and expertise to study nanotechnology within FDA’s Jefferson Laboratory Campus, including the National Center for Toxicological Research, and its consolidated headquarters at White Oak, Maryland. The Committee supports FDA in its mission to expand upon current research in nanotechnology and supports the development of a Nanotechnology Core Center to meet this mission. The Committee believes a Nanotechnology Core Center should be designed to support nanotechnology toxicity studies, develop analytical tools to quantify nanomaterials in complex matrices, and develop procedures for characterizing nanomaterials in FDA-regulated products. (p.82)

#### **FDA Action**

With Congressional support, FDA has strengthened its regulatory capability for the Agency’s Nanotechnology Regulatory Science Research Program by using a three-prong FDA-wide effort: (1) Development of a core infrastructure with equipment and expertise to provide FDA regulatory scientists with experience and knowledge in nanotechnology. This is demonstrated at FDA’s Jefferson’s Laboratories, nanotechnology facility which is fully operational and has been supporting FDA research and toxicology projects since 2010 and the co-development of a White Oak Campus nanotechnology facility supporting FDA characterization and manufacturing projects. (2) A training program provided by FDA review scientists and experts with laboratory experience with nanomaterials. This program was established in 2011. (3) Collaboration on regulatory science research projects addressing FDA’s regulatory needs. The FDA CORES program was established in 2011 and includes other US government agencies within the National Nanotechnology Initiative (NNI) and academic institutions. Investments to date have provided a sound base for FDA.

With continued investments, FDA will build upon the base that has been established for the Agency’s Nanotechnology Regulatory Science Research Program. The continued support will enable the agency to address questions related to the safety, effectiveness, product quality, and/or regulatory status of products that contain nanomaterials or otherwise involve the use of nanotechnology; develop models for safety and efficacy assessment; and study the behavior of nanomaterials in biological systems and their effects on human health.

**Item 30 – Obesity Therapeutics** – The Committee is concerned with the absence of novel medicines to treat obesity, the second leading cause of preventable deaths in the United States and a disease linked to cancer, high blood pressure, heart disease, diabetes, and stroke. With only diet, exercise, and gastric surgery as options, the lack of obesity medications is a significant unmet medical need. The Committee directs FDA to report by March 30, 2012 on the steps it will take to support the development of new treatments for obesity, including the use of its Risk Evaluation and Mitigation Strategy and other post-

marketing authorities, to mitigate risk and ensure rigorous post-market scrutiny while increasing access to novel medications. (p.82)

**FDA Action**

FDA will provide the report that the Committee requested.

**Item 31 – Office of Cosmetics and Colors [OCAC]**—The Committee provides not less than \$11,700,000 for cosmetics activities, including not less than \$7,200,000 for the Office of Colors and Cosmetics. Funding provided for OCAC is for direct support of the operation, staffing, compliance, research and international activities performed by this office. (p.82)

**FDA Action**

FDA will support this activity at the funding level provided by the Committee in FY 2012, subject to any changes to the FDA appropriation after the enactment of P.L. 112-55.

**Item 32 – Packaged Ice** – The Committee believes it is important that FDA provide guidance to manufacturers of packaged ice to ensure a safe product is sold to consumers. The Committee understands that a Citizens Petition was recently submitted to FDA regarding packaged ice, and encourages FDA to respond to this petition promptly. (p.82)

**FDA Action**

FDA received a petition on December 17, 2010 from the Packaged Ice Association that, among other things, asked FDA to establish a standard of identity (SOI) for packaged ice mirrored after the bottled water SOI. In the Statement of Grounds, the petitioner states concerns with the lack of inspection and no specific reference in FDA's regulations that identifies packaged ice as a food or establishes good manufacturing practices for packaged ice as the primary grounds for requesting an SOI.

FDA issued an interim response to the petitioner on June 17, 2011 indicating that we had not reached a decision on the petition in the first 180 days. We are still in the review/evaluation stage of the petition and have not yet reached a final decision. However, as noted in the petition, FDA did issue a food facts sheet clarifying that we do regulate packaged ice as a food. The full article is available at: <http://www.fda.gov/Food/ResourcesForYou/Consumers/ucm197586.htm>.

As resources permit, FDA plans to reach a final decision on this petition later this year.

**Item 33 – Seafood Advisory** – The Committee is concerned about differing messages from Federal agencies to pregnant women regarding the nutritional value of seafood consumption during pregnancy. The Committee directs FDA to initiate formal reconsideration of the 2004 advisory in consideration of the 2010 Dietary Guidelines. FDA shall report to the Committee within 120 days of enactment of this act on progress made and a timeline for final action on a new FDA advisory. (p.82)

**FDA Action**

FDA is discussing with the Environmental Protection Agency (EPA) an update of the 2004 advisory regarding the nutritional value of seafood consumption during pregnancy, in light of, among other things, a net benefits assessment conducted by FDA and the 2010 Dietary Guidelines. The agencies intend to issue a draft of an updated advisory early this year and then engage the public on this topic through public meetings and comments this year. This may include a consultation with the FDA Advisory Committee on Risk Communication. A report to Congress on reconsideration of the 2004 advisory was completed by CFSAN in September 2011 and submitted by HHS on December 29, 2011.

**Item 34 – Seafood Economic Integrity** – The Committee recognizes the importance of seafood to a healthy diet, but is concerned that FDA does not focus sufficient attention on economic integrity issues, particularly with respect to mislabeling of species, weights, country of origin, and treatment. The Committee encourages FDA to work with States and the Department of Commerce to more aggressively combat fraud in parts of the seafood industry. (p. 82)

**FDA Action**

For over 30 years, the Food and Drug Administration has been implementing systems and protocols with our State, territorial, tribal, and local regulatory partners to rapidly identify contaminated food via inspectional and sample analysis collaboration, determine the cause, and remove contaminated products from the marketplace. Within the Food Inspection State Contract Program, FDA currently collaborates with 24 states to perform 1131 Seafood HACCP inspections in which results and outcomes are shared with the respective FDA district offices. In the last 2 years, FDA has delivered 18 joint (FDA & State) Seafood Training courses. Along with HACCP food safety principles and label reviews, the joint training sessions include a dedicated section to economic fraud. The FDA also works closely with the National Fisheries Institute and NOAA's National Marine Fisheries Service to address economic fraud issues.

**Item 35 – Seafood Safety** – The Committee is aware that FDA currently inspects less than 2 percent of imported seafood. Further, many of these imports may contain substances that are banned in the United States. Therefore, the Committee directs FDA to develop a comprehensive program for imported

seafood, in accordance with the Food Safety Modernization Act, to ensure the safety of seafood. (p.83)

**FDA Action**

Since 1997, FDA has required all foreign seafood processors to implement seafood HACCP (Hazard Analysis Critical Control Point) programs for product intended for consumption in the United States. Foreign processors must address all food safety issues, implement safety controls, and maintain records of their activities as part of their HACCP program. FDA audits these programs during foreign facility inspections and as part of their importer verification procedures. Non-compliant processors or importers are banned from shipping product into the U.S. until corrections have been made.

In addition to the mandated HACCP programs, FDA has recently developed and utilized an electronic system (PREDICT) that prioritizes entries of imported seafood for sampling based on product risk. This allows FDA to focus available resources more effectively on products and processors that are more likely to submit adulterated foods for entry. Products that are unlikely or less likely to be adulterated receive a lower priority for sampling. The controls mandated by FSMA will further enhance the control of foreign sources of seafood and are currently under development, including third party accreditation of importers.

**Item – 36 – Trade Facilitation and Interagency Cooperation** – The current fiscal environment requires that efforts to enhance safety must be directed toward the most serious compliance infractions. The Committee strongly encourages FDA to establish a pilot project to expedite imports for highly compliant importers. The goal would be new trade facilitation methods for low-risk, shippers and cargo that could be incorporated into the import inspection process, thereby enabling FDA to better target Federal resources. FDA is strongly encouraged to provide clear guidelines for those shippers who are low-risk and to collaborate with industry, Customs and Border Protection and other relevant agencies on how such a program could be implemented. FDA is directed to provide a report to the Committee on its efforts in this regard within 120 days of enactment of this act. (p.83)

**FDA Action**

FDA will provide the report that the Committee requested.

**Conference Report Significant Items  
Contained in Conference Report 112-284  
To accompany H.R. 2112  
Date November 14, 2011**

**Item 37 – Administrative Savings** – The conference agreement includes the following increases: \$39,000,000 to begin implementation of the Food Safety Modernization Act; \$20,038,000 for advancing medical countermeasures...the conferees direct FDA to provide a report within 30 days of enactment of this Act on how it intends to allocate these increases. (p.185)

**FDA Action**

On January 5, 2012 and January 3, 2012, FDA provided the reports that the Committee requested.

**Item 38 – Pre-Market Approval Times** - The conferees direct that, within 90 days of the date of enactment of this Act, FDA report on the average number of calendar days that elapsed from the date that drug applications (including any supplements) were submitted to the agency under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) until the date that the drugs were approved; the average number of calendar days that elapsed from the date that applications for device clearance (including any supplements) under section 510(k) of the FD&C Act or for premarket approval (including any supplements) under section 515 of the FD&C Act were submitted to the agency until the date that the devices were cleared; and the average number of calendar days that elapsed from the date that biological license applications (including any supplements) were submitted to the agency under section 351 of the Public Health Service Act until the date that the biological products were licensed. (p. 186) (Office of Planning)

**FDA Action**

FDA will provide the report that the Committee requested.

**Item 39 – OTC Cold Medicines for Children** - The conferees are concerned that FDA has not issued a proposed rule revising the monograph regulating the labeling of over-the-counter cough and cold products for children. The conferees direct the FDA to publish a proposed rule by December 31, 2011, based on the latest scientific evidence for safety and efficacy in pediatric populations. (p.186) (

**FDA Action**

FDA acknowledges the importance of issuing a proposed rule addressing potential changes to the labeling of over-the-counter cold and cough products for use in children. Although the changes being considered are very complex and

require appropriate justifications, the FDA is working expeditiously to issue this proposed rule.

**Item 40 – Nanotechnology** - The conferees recognize that FDA is developing facilities and expertise to study nanotechnology within FDA's Jefferson Laboratory Campus, including the National Center for Toxicological Research, and its consolidated headquarters at White Oak, Maryland. The conferees support FDA in its mission to expand upon current research in nanotechnology and support the eventual development of a Nanotechnology Core Center to meet its mission. (p. 186) (OCS [lead], in consultation with NCTR)

#### **FDA Action**

FDA investments will continue to enable the agency to address questions related to the safety, effectiveness, product quality, and/or regulatory status of products that contain nanomaterials or otherwise involve the use of nanotechnology; develop models for safety and efficacy assessment; and study the behavior of nanomaterials in biological systems and their effects on human health. FDA will continue activities that meet the following FDA-wide priorities: (1) scientific staff development and professional training, (2) laboratory and product testing capacity, and (3) collaborative and interdisciplinary research to address product characterization and safety.

**Item 41 – Imported Seafood** - The conferees are aware that FDA currently inspects less than 2 percent of imported seafood. Further, many of these imports may contain substances that are banned in the United States. Therefore, the conferees direct FDA to develop a comprehensive program for imported seafood. (p.186)

#### **FDA Action**

Since 1997, FDA has required all foreign seafood processors to implement seafood HACCP (Hazard Analysis Critical Control Point) programs for product intended for consumption in the United States. Foreign processors must address all food safety issues, implement safety controls, and maintain records of their activities as part of their HACCP program. FDA audits these programs during foreign facility inspections and as part of their importer verification procedures. Non-compliant processors or importers are banned from shipping product into the U.S. until corrections have been made.

In addition to the mandated HACCP programs, FDA has recently developed and utilized an electronic system (PREDICT) that prioritizes entries of imported seafood for sampling based on product risk. This allows FDA to focus available resources more effectively on products and processors that are more likely to submit adulterated foods for entry. Products that are unlikely or less likely to be

adulterated receive a lower priority for sampling. The controls mandated by FSMA will further enhance the control of foreign sources of seafood and are currently under development, including third party accreditation of importers.

**Item 42 – Approval Process transparency** - The conferees emphasize the importance of predictability and transparency in the FDA approval process, and urge FDA to remain focused on its core mission of ensuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, fostering the development of medical products to support the counterterrorism effort, and helping to speed innovation of safe and effective products that improve the lives of patients and consumers. The conferees urge FDA to be responsive, timely, and transparent throughout the approval process for all human and veterinary drugs, biological products, medical devices, and medical countermeasures.

#### **FDA Action**

The Centers for Drugs, Biologics, and Devices and Radiologic are committed to predictability, consistency, and transparency of their respective review processes, including training of reviewers, interaction with sponsors, and implementation and tracking of policies to ensure the highest quality and timeliness of regulatory science.

**Item 43 – Food Safety** – The conferees note that the most recent CDC estimates are that only 20 percent of foodborne illnesses are from 31 known pathogens such as norovirus, salmonella and clostridium. Since 80 percent of illnesses are caused by unknown sources, FDA is encouraged to work with the public and private sectors to gain a better understanding of the causes of illness. FDA's broader understanding of unknown sources should contribute towards the development of new strategies, policies, and foodborne illness prevention methods. While simultaneously seeking answers to unknown sources and plans to address these hazards, FDA has to do a better job of identifying more effective food safety activities that will reduce illnesses, hospitalizations, and deaths associated with the other 20 percent of foodborne illness. Within the funding level for food safety, FDA is directed to develop a clear strategy on how the agency can prioritize intervention methods along the farm to fork continuum to reduce illness once they have discovered the sources for a much greater proportion of unknown agents and to tie the funding levels for food safety to increased levels of activities to both the known and the unknown sources of illness. The conferees direct FDA to include this information in the fiscal year 2013 budget justifications to Congress. (p.186)

#### **FDA Action**

FDA has included information on its food safety strategy in the fiscal year 2013 budget justifications to Congress.